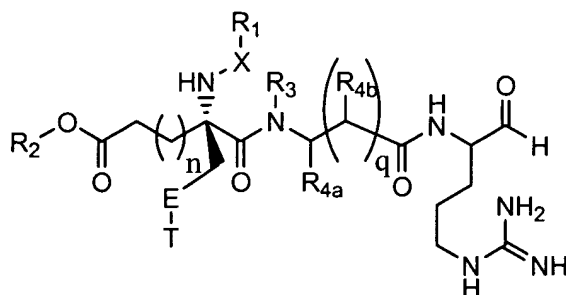


Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1. (Original) A compound of the formula:



wherein:

(a) X is selected from the group consisting of $-C(=O)-$, $-C(=O)-O-$, $-C(=O)NH-$, $-S(O)_2-$, $-S(O)_2NH-$ and a direct link;

(b) R_1 is selected from the group consisting of

(1) alkyl of 1 to about 12 carbon atoms which is unsubstituted or substituted with 1 or 2 substituents selected from the group consisting of Y_1 and Y_2 ;

(2) alkyl of 1 to about 3 carbon atoms substituted with cycloalkyl of 3 to about 8 carbon atoms which is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of Y_1 , Y_2 and Y_3 ;

(3) cycloalkyl of 3 to about 8 carbon atoms which is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of Y_1 , Y_2 and Y_3 ; and

(4) aryl of about 6 to 14 carbon atoms which is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of Y_1 , Y_2 and Y_3 ;

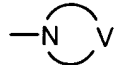
(5) aralkyl of about 7 to about 15 carbon atoms which is unsubstituted or substituted on the alkyl chain with hydroxy or halogen and which is unsubstituted or substituted on the aryl ring

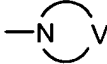
with 1 to 3 substituents selected from the group consisting of Y_1 , Y_2 and Y_3 ;

(6) hydrogen when X is $-C(=O)NH-$, $-S(O)_2-$, $-S(O)_2NH-$, or a direct link;

(7) heterocycloalkyl of 4 to about 10 ring atoms with the ring atoms selected from carbon and heteroatoms, wherein the heteroatoms are selected from the group consisting of oxygen, nitrogen, and $S(O)_i$, wherein i is 0, 1 or 2, which is unsubstituted or mono-, di-, or tri-substituted on the ring with 1 to 3 substituents selected from the group consisting of Y_1 , Y_2 , and Y_3 ;

(8) heterocyclo of 4 to about 10 ring atoms with the ring atoms selected from carbon and heteroatoms, wherein the heteroatoms are selected from the group consisting of oxygen,

nitrogen, and $S(O)_i$, wherein i is 0, 1, or 2, including, 

wherein  is a 5 to 7 member heterocycle having 3 to 6 ring carbon atoms, where V is $-CH_2-$, $-O-$, $-S(=O)-$, $-S(O)_2-$ or $-S-$, which is unsubstituted or mono-, di-, or tri-substituted on the ring carbons with 1 to 3 substituents selected from the group consisting of Y_1 , Y_2 , and Y_3 ;

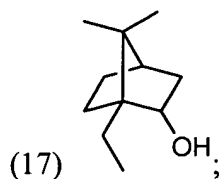
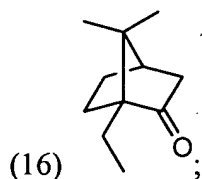
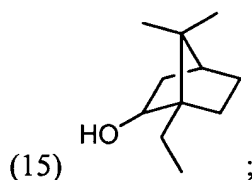
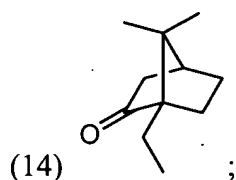
(9) alkenyl of 2 to 6 carbon atoms which is unsubstituted or substituted with cycloalkyl of 3 to 8 carbon atoms, which is unsubstituted or mono-, di-, or tri-substituted on the ring with 1 to 3 substituents selected from the group consisting of Y_1 , Y_2 , and Y_3 ;

(10) heteroaryl of 5 to 14 ring atoms with the ring atoms selected from carbon and heteroatoms, wherein the heteroatoms are selected from oxygen, nitrogen, and sulfur, and which is unsubstituted or mono-, di- or tri-substituted with 1 to 3 substituents selected from the group consisting of Y_1 , Y_2 , and Y_3 ;

(11) heteroaralkyl of about 5 to about 14 ring atoms with the ring atoms selected from carbon and heteroatoms, wherein the heteroatoms are selected from oxygen, nitrogen, and sulfur, which is unsubstituted or substituted on the alkyl chain with hydroxy or halogen and which is unsubstituted on the ring or mono-, di- or tri-substituted on the ring with 1 to 3 substituents selected from the group consisting of Y_1 , Y_2 , and Y_3 ;

(12) aralkenyl of about 8 to about 16 carbon atoms which is unsubstituted or mono-, di-, or tri-substituted on the aryl ring with 1 to 3 substituents selected from the group consisting of Y₁, Y₂, and Y₃;

(13) heteroaralkenyl of 5 to 14 ring atoms with the ring atoms selected from carbon and heteroatoms, wherein the heteroatoms are selected from oxygen, nitrogen, and sulfur, and which is unsubstituted or mono-, di- or tri-substituted on the ring carbons with 1 to 3 substituents selected from the group consisting of Y₁, Y₂, and Y₃;



(18) fused carbocyclic alkyl of about 9 to about 15 carbon atoms;

(19) difluoromethyl or perfluoroalkyl of 1 to about 12 carbon atoms;

(20) perfluoroaryl of about 6 to about 14 carbon atoms; and

(21) perfluoroaralkyl of 7 to 15 carbon atoms., and wherein each Y_1 , Y_2 , and Y_3 is independently selected and is

(i) selected from the group consisting of halogen, cyano, nitro, tetrazolyl, guanidino, amidino, methylguanidino, $-\text{CF}_3$, $-\text{CF}_2\text{CF}_3$, $-\text{CH}(\text{CF}_3)_2$, $-\text{C}(\text{OH})(\text{CF}_3)_2$, $-\text{OCF}_3$, $-\text{OCF}_2\text{H}$, $-\text{OCF}_2\text{CF}_3$, $-\text{OC}(\text{O})\text{NH}_2$, $-\text{OC}(\text{O})\text{NHZ}_1$, $-\text{OC}(\text{O})\text{NZ}_1\text{Z}_2$, $-\text{NHC}(\text{O})\text{Z}_1$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHC}(\text{O})\text{NZ}_1$, $-\text{NHC}(\text{O})\text{NZ}_1\text{Z}_2$, $-\text{C}(\text{O})\text{OH}$, $-\text{C}(\text{O})\text{OZ}_1$, $-\text{C}(\text{O})\text{NH}_2$, $-\text{C}(\text{O})\text{NHZ}_1$, $-\text{C}(\text{O})\text{NZ}_1\text{Z}_2$, $-\text{P}(\text{O})_3\text{H}_2$, $-\text{P}(\text{O})_3(\text{Z}_1)_2$, $-\text{S}(\text{O})_3\text{H}$, $-\text{S}(\text{O})_m\text{Z}_1$, $-\text{Z}_1$, $-\text{OZ}_1$, $-\text{OH}$, $-\text{NH}_2$, $-\text{NHZ}_1$, $-\text{NZ}_1\text{Z}_2$, $-\text{C}(=\text{NH})\text{NH}_2$, $-\text{C}(=\text{NOH})\text{NH}_2$, $-\text{N-morpholino}$, and $-\text{S}(\text{O})_m(\text{CF}_2)_q\text{CF}_3$, wherein m is 0, 1 or 2, q is an integer from 0 to 5, and Z_1 and Z_2 are independently selected from the group consisting of alkyl of 1 to about 12 carbon atoms, aryl of about 6 to about 14 carbon atoms, heteroaryl of 5 to about 14 ring atoms, aralkyl of 7 to 15 carbon atoms, and heteroaralkyl of 5 to about 14 ring atoms, or

(ii) Y_1 and Y_2 are selected together to be $-\text{O}[\text{C}(\text{Z}_3)(\text{Z}_4)]_r\text{O}$ or $-\text{O}[\text{C}(\text{Z}_3)(\text{Z}_4)]_{r+1}-$, wherein r is an integer from 1 to 4 and Z_3 and Z_4 are independently selected from the group consisting of hydrogen, alkyl of 1 to about 12 carbon atoms, aryl of about 6 to about 14 carbon atoms, heteroaryl of about 5 to about 14 ring atoms, aralkyl of about 7 to about 15 carbon atoms, and heteroaralkyl of about 5 to about 14 ring atoms;

(c) R_2 is hydrogen or alkyl of 1 to 12 carbon atoms;

(d) n is 0, 1, 2 or 3;

(e) R_3 is hydrogen or methyl or R_3 , R_{4a} and q are selected together as set forth in (g);

(f) R_{4a} and R_{4b} are independently hydrogen, lower alkyl of 1 to 3 carbon atoms, and q is 0, 1 or 2, or R_3 , R_{4a} and q are selected together as set forth in (g);

(g) q is 0 and R_3 and R_{4a} are selected together to be in the S-configuration to give a group at P2 selected from the group consisting of prolyl, pipecolyl, azetidine-2-carbonyl; 4-hydroxyprolyl, 3-hydroxyprolyl, 4-aminoprolyl, 4-(CH_2NH_2)-prolyl, 3, 4-methanoprolyl and 3,4-dehydroprolyl;

(h) E is a 5- or 6-membered aromatic ring having 0 to 2 ring heteroatoms and the remainder of the ring atoms carbon atoms,

wherein the heteratoms are selected from the group consisting of oxygen, nitrogen and sulfur, and which is substituted with R₅ and R₆ wherein R₅ and R₆ are independently selected from the group consisting of hydrogen, , hydroxy, halogen, alkyl of 1 to about 6 carbon atoms, alkyl of 1 to about 4 carbon atoms substituted with alkoxy of 1 to about 4 carbon atoms, alkoxy of 1 to about 6 carbon atoms and trifluoromethyl; and

(i) T is hydrogen, hydroxy, -CH₂OH, alkyl of 1 to about 3 carbon atoms, cyano, -C(=NR₇)NHR₈ -NH-C(=NR₇)NHR₈, -NHR₉, or -C(=O)NHR₉ wherein R₇ and R₈ are independently hydrogen, hydroxy, alkoxy of 1 to about 3 carbon atoms, trihydrocarbosilyl of 3 to about 16 carbon atoms, alkyl of 1 to about 3 carbon atoms or -C(=O)R₉ wherein R₉ is hydrogen, alkyl of 1 to about 6 carbon atoms, alkoxy of 1 to about 6 carbon atoms or -(CF₂)_jCF₃ wherein j is 0, 1, 2 or 3, and with the proviso that R₇ and R₈ are not both hydroxy or alkoxy; and pharmaceutically acceptable salts thereof.

2. (Original) A compound according to claim 1 wherein q is 0.

3. (Original) A compound according to claim 2 wherein n is 0 or 1.

4. (Original) A compound according to claim 3 wherein R₃ is hydrogen.

5. (Original) A compound according to claim 4 wherein R_{4a} is hydrogen or methyl.

6. (Original) A compound according to claim 5 wherein R₂ is hydrogen or methyl.

7. (Original) A compound according to claim 6 wherein X is a direct link, -S(O)₂-, -C(=O)O-, or -C(=O)NH-.

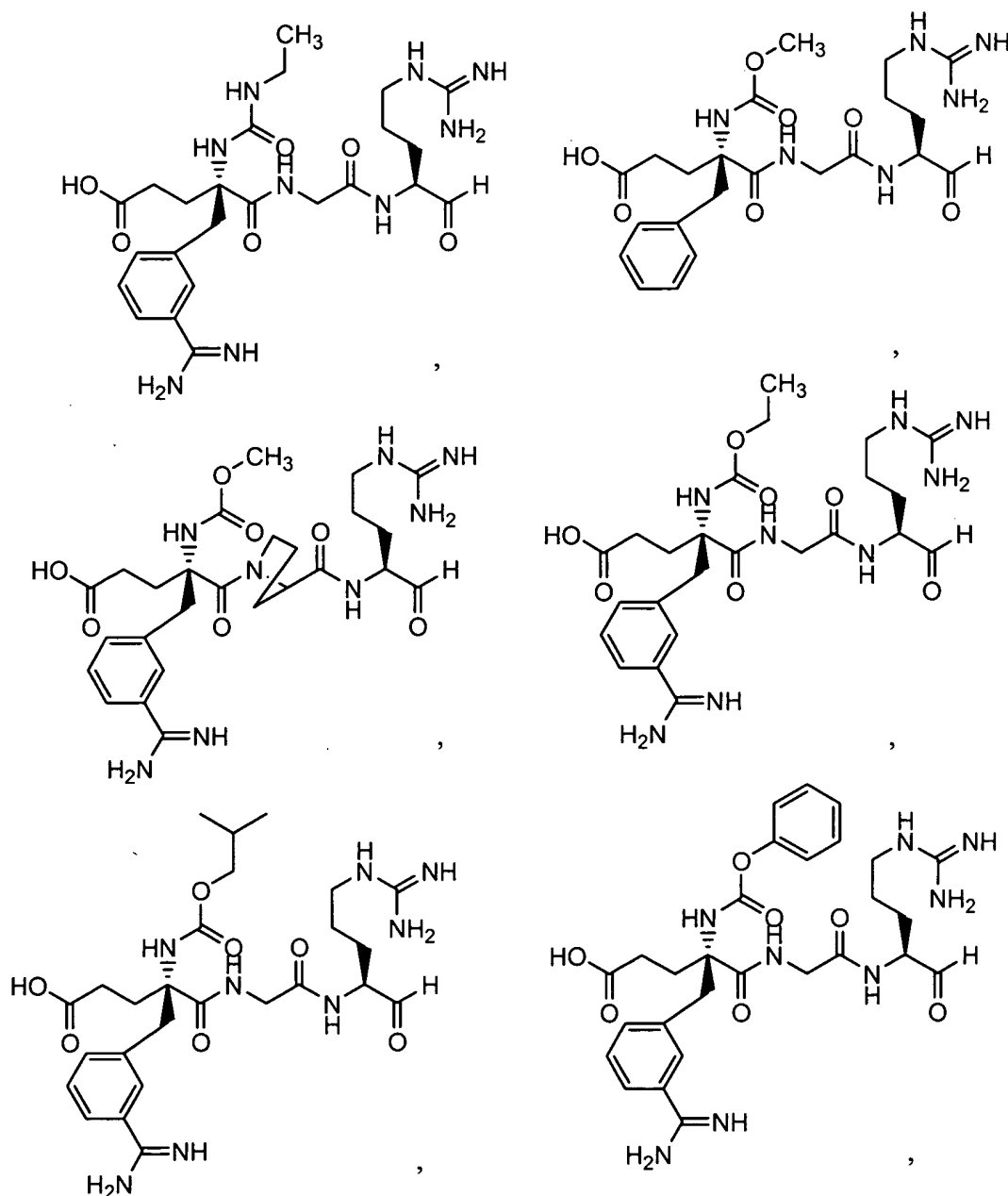
8. (Withdrawn) A compound according to claim 7 wherein X is a direct link.

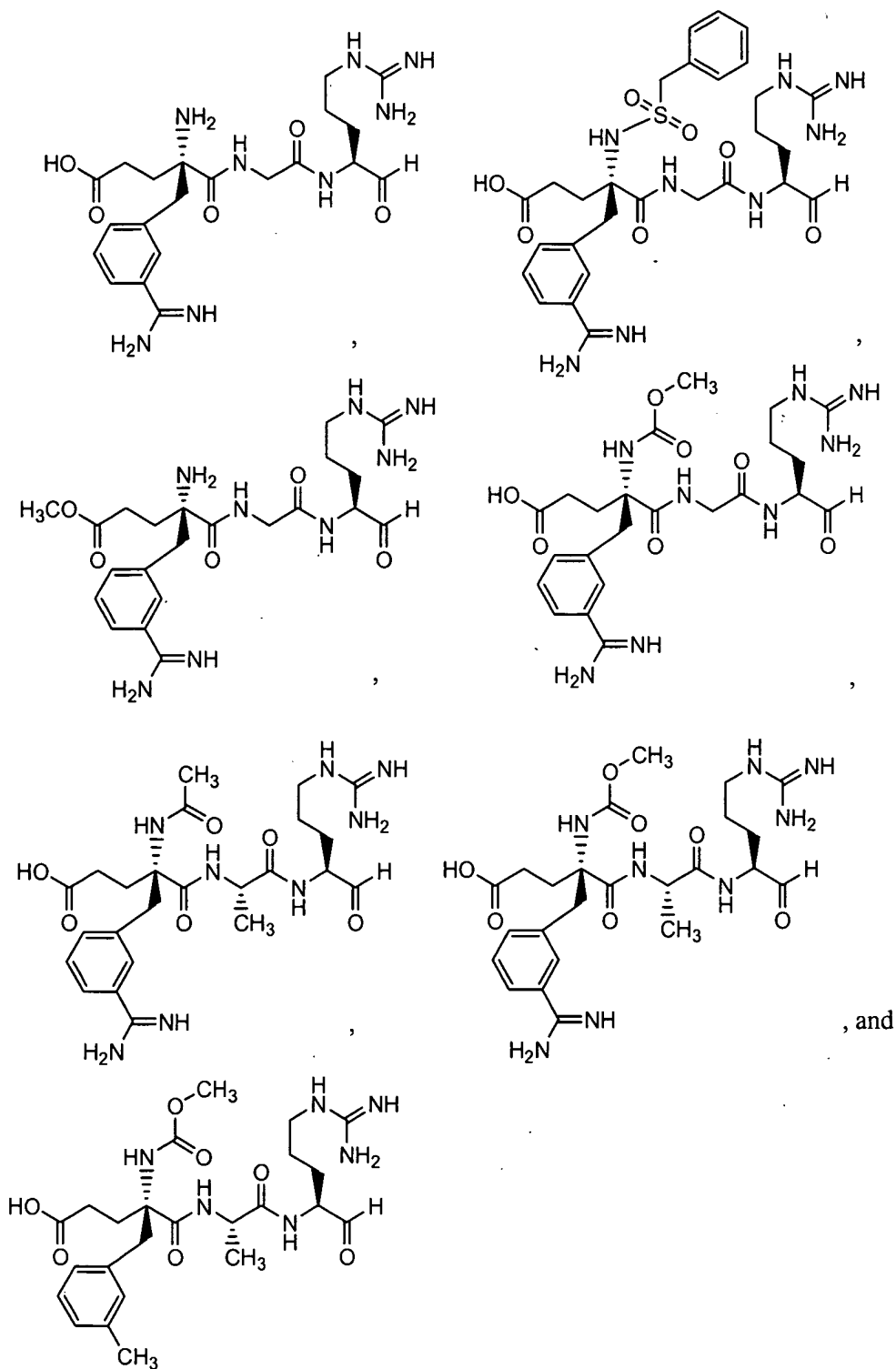
9. (Withdrawn) A compound according to claim 8 wherein R₁ is hydrogen.

10. (Withdrawn) A compound according to claim 7 wherein X is -S(O)₂-.

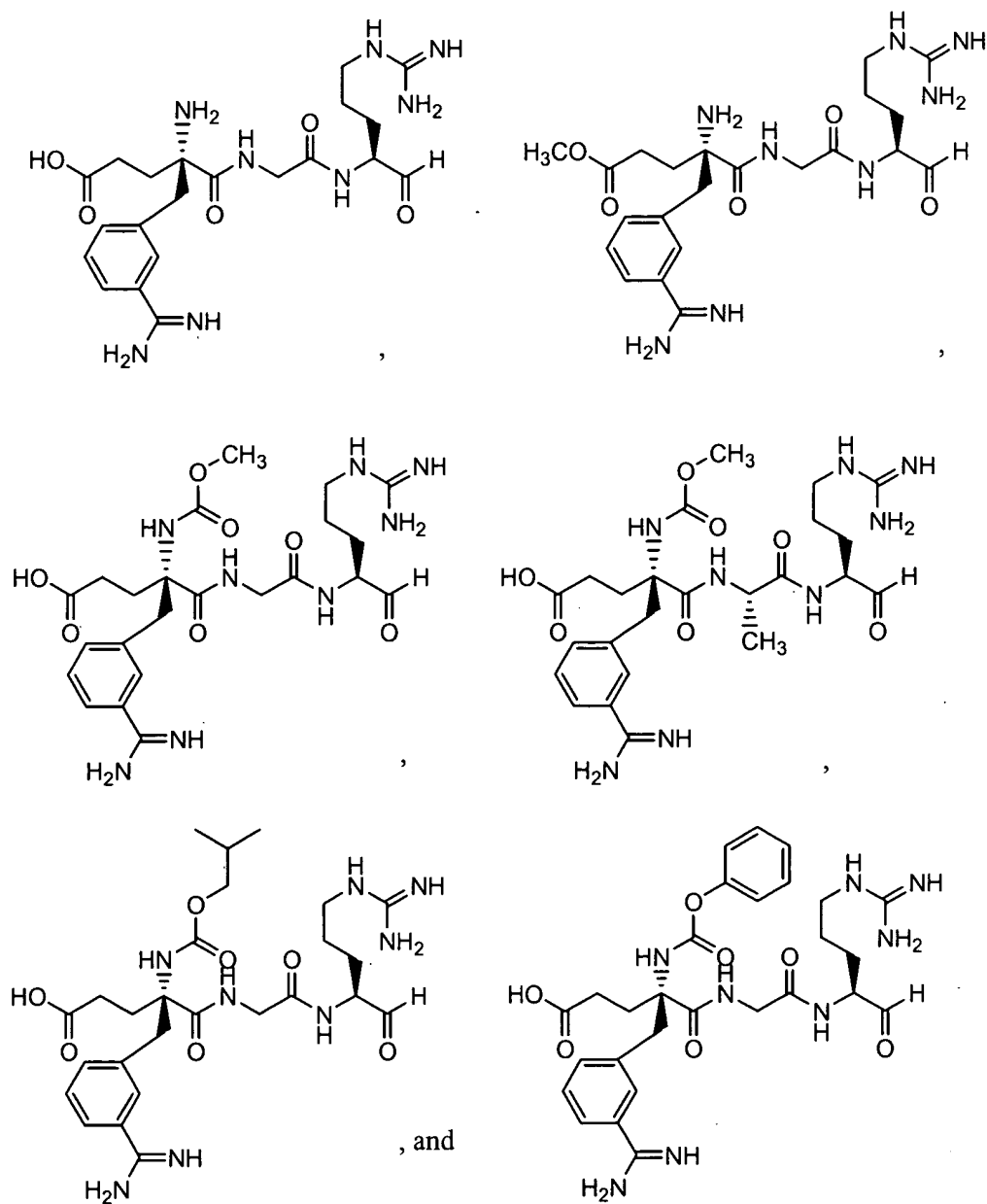
11. (Withdrawn) A compound according to claim 10 wherein R_1 is aralkyl.
12. (Original) A compound according to claim 7 wherein X is $-C(=O)O-$.
13. (Original) A compound according to claim 12 wherein R_1 is alkyl.
14. (Original) A compound according to claim 7 wherein E is phenyl.
15. (Original) A compound according to claim 14 wherein T is $-C(=NR_7)NHR_8$.
16. (Original) A compound according to claim 15 wherein R_7 and R_8 are hydrogen.
17. (Withdrawn) A compound according to claim 3 wherein R_3 and R_{4a} are selected together as set forth in (g) of claim 1.
18. (Original) A compound according to claim 2 wherein E is phenyl.
19. (Withdrawn) A compound according to claim 18 wherein X is a direct link and R_1 is hydrogen.
20. (Withdrawn) A compound according to claim 19 wherein R_2 is hydrogen or alkyl of 1 to about 3 carbons.
21. (Original) A compound according to claim 18 wherein T is $-C(=NR_7)NH R_8$.
22. (Original) A compound according to claim 21 wherein R_7 and R_8 are hydrogen.
23. (Original) A compound according to claim 1 wherein E is phenyl.
24. (Withdrawn) A compound according to claim 23 wherein R_3 and R_{4b} are hydrogen and R_{4a} is hydrogen or methyl or q, R_3 and R_{4a} are taken together as in (g) of claim 1.

25. (Currently amended) A compound according to claim 1 selected from the group consisting of ~~the compounds depicted in Figures 5A and 5B:~~





26. (Currently amended) A compound according to claim 1 selected from the group consisting of ~~Compounds A, C, D, F, I and M depicted in Figures 5A and 5B:~~



27. (Currently amended) A pharmaceutical composition which comprises an amount effective to inhibit or decrease serine protease activity of matriptase or MTSP1 of a compound of any of claims 1 to 26.

28. (Original) A method of treating a pathologic condition in a mammal which is ameliorated by decreasing or inhibiting the serine protease activity of matriptase or MTSP1 which comprises administering to said mammal an amount of a compound of any of claims 1 to 26 effective to decrease or inhibit serine protease activity of matriptase of MTSP1.

29. (Original) A method of treating a pathologic condition in a mammal which is ameliorated by decreasing or inhibiting the serine protease activity of matriptase or MTSP1 which comprises administering to said mammal an amount of a composition of claim 27 effective to decrease or inhibit serine protease activity of matriptase of MTSP1.

30. (Original) A method of treating a condition which is ameliorated by inhibiting or decreasing serine protease activity of matriptase or MTSP1 in a mammal which comprises administering to said mammal an therapeutically effective amount of a compound which inhibits serine protease activity of matriptase of MTSP1.

31. (Original) A method according to claim 30 wherein said compound has an IC_{50} of 100 nM or less.

32. (Cancel).

33. (Original) A method of treating a condition which is ameliorated by inhibiting or decreasing serine protease activity of matriptase or MTSP1 in a mammal in need of treatment which comprises administering to said mammal a therapeutically effective amount of a compound which selectively inhibits serine protease activity of matriptase or MTSP1.

34. (Cancel).

35. (Cancel).

36. (Cancel).